

ND WT

3. (Amended three times) A method for generating an adenoviral vector comprising welding together two nucleic acid molecule in a cell wherein both nucleic acid molecule of said two nucleic acid molecules comprise only one adenovirus inverted terminal repeat or a part thereof having the function of an inverted terminal repeat, said two nucleic acid molecules further comprising partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof, wherein the two nucleic acid molecules present in the cell do not include sequence overlap leading to the formation of replication competent adenovirus.

DD

6. (Amended three times) A method for generating an adenoviral vector comprising welding together two nucleic acid molecules in a mammalian cell wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; wherein said two nucleic acid molecules are not capable of replicating in said mammalian cell prior to said welding together, and wherein the two nucleic acid molecules present in the mammalian cell do not include sequence overlap leading to the formation of replication competent adenovirus.

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8. (Twice amended) A method for generating an adenoviral vector comprising welding together two nucleic acid molecules in a cell, wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid of interest or functional parts thereof and wherein at least one nucleic acid molecule of said two nucleic acid molecules provided to said cell comprises an adenovirus inverted terminal repeat which, on one side, is essentially free of other nucleic acid.

10. (Twice amended) A method for generating an adenoviral vector comprising welding together two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof, wherein at least one nucleic acid molecule of said two nucleic acid molecules comprises an adenovirus inverted terminal repeat made essentially free of other nucleic acid on one side using a restriction enzyme that acts on a site which is not present in adenoviral vector nucleic acid in said at least one nucleic acid molecule.

13. (Three times amended) A method for generating an adenoviral vector comprising welding together, in a PER.C6 cell (ECACC 96022940), two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof, and wherein the two nucleic acid molecules present in the cell do not include sequence overlap leading to the formation of replication competent adenovirus.

14. (Three times amended) A method for generating an adenoviral vector comprising welding together, in a cell, two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and nucleic acid sequence of interest or functional parts thereof; said physically linked nucleic acid in said cell further comprising a nucleic acid sequence encoding an adenoviral E2-region and/or an adenoviral E4-region protein, and wherein the two nucleic acid molecules present in the cell do not include sequence overlap leading to the formation of replication competent adenovirus.

60. (Amended) A method for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences of each nucleic acid molecule of said two nucleic acid molecules comprise essentially only one continuous sequence such that homologous recombination may occur leading to the generation of physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid of interest or functional part thereof, wherein said welding together is performed in a cell or a functional part thereof.

62. (Twice amended) A method for generating an adenoviral vector comprising welding together, through homologous recombination in a mammalian cell, two nucleic acid molecules incapable of replicating in said mammalian cell prior to said welding together; said two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences on each nucleic acid molecule of said two nucleic acid molecules comprise essentially only one continuous sequence such that homologous recombination may occur, leading to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof, and wherein the two nucleic acid molecules present in the cell do not include sequence overlap leading to the formation of replication competent adenovirus.

66. (Twice amended) A method for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences of each nucleic acid molecule of said two nucleic acid molecules comprise essentially only one continuous sequence such that homologous recombination may occur, leading to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof, at least one nucleic acid molecule of said two nucleic acid molecules provided to said cell comprises an adenovirus inverted terminal repeat which, on one side, is made essentially free of other nucleic acid using a restriction enzyme

D8) that acts on a site which is not present in adenoviral vector nucleic acid in said at least one nucleic acid molecule.

D9 69. (Twice amended) A method for generating an adenoviral vector comprising welding together, through homologous recombination in a PER.C6 cell (ECACC 96022940), two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences of each nucleic acid molecule comprise essentially only one continuous sequence such that homologous recombination may occur, leading to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof, and wherein the two nucleic acids present in the cell do not include sequence overlap leading to the formation of replication competent adenovirus.

70. (Twice amended) A method for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences of each nucleic acid molecule of said two nucleic acid molecules comprise essentially only one continuous sequence such that homologous recombination may occur, leading to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid sequence of interest or functional parts thereof; said physically linked nucleic acid further comprising a nucleic acid sequence encoding an adenoviral E2-region and/or an adenoviral E4-region protein, and wherein the two nucleic acids present in the cell do not include sequence overlap leading to the formation of replication competent adenovirus.

D10 72. (Twice amended) A method for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences of each nucleic acid molecule of said two nucleic acid molecules comprise essentially only one continuous sequence such that homologous recombination may occur, leading to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and

a nucleic acid sequence of interest or functional parts thereof; at least one nucleic acid molecule of said two nucleic acid molecules comprising an adenoviral capsid protein encoding nucleic acid derived from two different adenovirus serotypes.

73. (Twice amended) A method for generating an adenoviral vector comprising welding together through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences of each nucleic acid molecule of said two nucleic acid molecules comprise essentially only one continuous sequence whereby homologous recombination may occur, leading to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal, a nucleic acid encoding at least one adenoviral E1-region protein, at least one adenoviral E2-region encoded protein and/or at least one adenoviral E4-region encoded protein and a nucleic acid sequence of interest or functional parts thereof and wherein at least one of said E1-region encoded proteins is under transcriptional control of a conditionally active promoter.

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